REMARKS

The Office Action dated July 15, 2008 has been received and reviewed. Prior to the present communication, claims 1-3, 6-12, 15-17, 20, 24, and 27 were pending in the subject application. Claim 3 has been canceled herein, and each of claims 1, 2, 6, 8-10, 12, 16, 17 and 24 has been amended. As such, claims 1, 2, 6-12, 15-17, 20, 24 and 27 remain pending Applicants submit that no new matter has been added by way of these amendments. Reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

Objections

Claims 1, 6, 7, and 12 have been objected to based upon some inadvertent informalities. More particularly, the phrase "measuring the sample contains for" is objected to in claim 1; claims 6 and 7 are objected to for being in improper dependent form; and claim 12 is objected to due to the phrase "bind to captured lactoferrin." *See*, Office Action at page 15, ¶ 26. Applicants respectfully submit that the noted informalities have been corrected herein and, as such, the objection to these claims has been overcome.

Double Patenting

Claims 1, 3, 11-12, 15-16 and 24 have been provisionally rejected on the ground of non-statutory obviousness-type double patenting over claims 1-2 of co-pending Application No. 2004/0033537. *See*, Office Action at page 4, ¶ 6. The rejection is hereby traversed and Applicants respectfully request that the grounds of rejection be held in abeyance until allowable subject matter is indicated.

Claims 1, 3, 11-12, 15-16 and 24 have been provisionally rejected on the ground of non-statutory obviousness-type double patenting over claims 1-14 of U.S. Patent No.

7,192,724. *See*, Office Action at page 4, ¶ 8. The rejection is hereby traversed and Applicants respectfully request that the grounds of rejection be held in abeyance until allowable subject matter is indicated.

Claims 1-3, 6-12, 15-17 and 20 have been provisionally rejected on the ground of non-statutory obviousness-type double patenting over claims 1-3 and 7-14 of co-pending Application No. PG-pub 2004, 0126898. *See*, Office Action at page 5, ¶ 10. The rejection is hereby traversed and Applicants respectfully request that the grounds of rejection be held in abeyance until allowable subject matter is indicated.

Rejections based on 35 U.S.C. § 112

Claim 8 has been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More particularly, the phrase "capturing fragments" has been rejected as being unclear. *See*, Office Action at page 3, ¶ 4. Claim 8 has been amended as set forth herein above. Applicants respectfully submit that the amendment overcomes the 35 U.S.C. § 112, second paragraph, rejection of claim 8. As such, Applicants respectfully request withdrawal of the rejection of claim 8 under 35 U.S.C. §112, second paragraph.

Rejections based on 35 U.S.C. § 102

A. Applicable Authority.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdeggal Brothers v. Union Oil Co. of California*, 814 F.2d 628, 631 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . .

claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 2 USPQ 2d 1913, 1920 (Fed. Cir. 1989). *See also*, MPEP §2131.

B. Anticipation Rejections Based on the Guerrant Reference (U.S. Patent 5,124,252).

Claims 1, 3, 8-11, 15 and 24 have been rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,124,252 to Guerrant et al. (hereinafter the "Guerrant reference"). *See*, Office Action at page 5, ¶12. As the Guerrant reference fails to describe, either expressly or inherently, each and every element of the rejected claims, and further fails to disclose the identical invention in the detail contained in the claims, Applicants respectfully traverse the rejection.

Independent claim 1, as amended herein, is directed to a method for testing fecal samples from persons for diagnosis. The method comprises obtaining a fecal sample from a person presenting with symptoms common to inflammatory bowel disease and irritable bowel syndrome, determining that the sample contains an elevated level of lactoferrin, and measuring the sample for an elevated level of anti-*Saccharomyces cerevisiae* antibodies (ASCA) and an elevated level of anti-neutrophil cytoplasmic antibodies (ANCA). Upon determining that the sample has an elevated level of anti-*Saccharomyces cerevisiae* antibodies and not an elevated level of anti-neutrophil cytoplasmic antibodies, the patient is diagnosed with Crohn's disease. In contrast, upon determining that the sample has an elevated level of anti-neutrophil cytoplasmic antibodies and not an elevated level of anti-*Saccharomyces cerevisiae* antibodies, the patient is diagnosed with ulcerative colitis.

Independent claim 24, as amended herein, is directed to a method for distinguishing inflammatory bowel disease from irritable bowel syndrome and for differentiating

ulcerative colitis from Crohn's disease. The method comprises obtaining a fecal sample from a person presenting with symptoms common to inflammatory bowel disease and irritable bowel syndrome and measuring the sample for an elevated or non-elevated level of lactoferrin. Upon determining that the sample has a non-elevated level of lactoferrin, the person is diagnosed with irritable bowel syndrome. Conversely, upon determining that the sample has an elevated level of lactoferrin, the sample is selected for further measurements. The selected sample is measured for an elevated level of anti-*Saccharomyces cerevisiae* antibodies (ASCA) and an elevated level of anti-neutrophil cytoplasmic antibodies (ANCA). Upon determining that the seleted sample has an elevated level of anti-*Saccharomyces cerevisiae* antibodies and not an elevated level of anti-neutrophil cytoplasmic antibodies, the patient is diagnosed with Crohn's disease. In contrast, upon determining that the selected sample has an elevated level of anti-neutrophil cytoplasmic antibodies and not an elevated level of anti-*Saccharomyces cerevisiae* antibodies, the patient is diagnosed with ulcerative colitis.

The Guerrant reference, on the other hand, discloses only obtaining a fecal sample from a person and determining whether lactoferrin is present in the sample. It does not disclose determining whether the obtained fecal sample contains an elevated level of either ASCA and ANCA, nor does it disclose diagnosing a patient based upon elevated levels of either ASCA or ANCA. As such, it is respectfully submitted that the Guerrant reference fails to anticipate independent claims 1 or 24. It is stated in the Office Action that claims 1 and 24 "only carr[y] out the determining steps for ASCA and ANCA when the lactoferrin determination is positive and elevated." *See,* Office Action at page 7, ¶ 15. Applicants respectfully submit, however, that the determinations regarding the presence of elevated ASCA and ANCA are not optional in claims 1 and 24, as amended herein. As such, to anticipate these claims, the Guerrant reference

must describe, either expressly or inherently, not only measuring a sample for elevated levels of ASCA and ANCA, but also diagnosing a person from whom the tested sample was obtained based upon the results of such measurements. The Guerrant reference fails on both accounts. As such, it is respectfully submitted that the Guerrant reference fails to anticipate these claims.

Each of claims 8-11 and 15 depends directly or indirectly from claim 1. As such, Applicants respectfully submit that these claims are not anticipated by the Guerrant reference for at least the above-cited reasons. Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejection of claims 1, 8-11 and 15 based upon the Guerrant reference. Claim 3 has been cancelled by way of the present communication and, accordingly, the rejection of this claim has been rendered moot.

C. Anticipation Rejections Based on the Fine Reference (*American Journal of Gastroenterology*, Vol. 93, No. 8, pp 1300-1305, 1998).

Claims 1, 3, 11, 24 and 27 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Fine et al. (American Journal of Gastroenterology, Vol. 93, No. 8, pp 1300-1305, 1998 (hereinafter the "Fine reference"). *See*, Office Action at page 8, ¶ 19. As the Fine reference fails to describe, either expressly or inherently, each and every element as set forth in the rejected claims, Applicants respectfully traverse this rejection.

As previously discussed, amended claims 1 and 24 each require determining that a sample contains an elevated level of ASCA or ANCA and diagnosing the person from whom the sample was obtained based upon such determination. The Fine reference, on the other hand, discloses only a method of obtaining a fecal sample from a person and determining whether lactoferrin is present in the sample. The Fine reference does not describe, either expressly or inherently determining whether the obtained fecal sample contains an elevated level of either

ASCA and ANCA, nor does it disclose diagnosing a patient based upon elevated levels of either ASCA or ANCA. As such, it is respectfully submitted that the Fine reference fails to anticipate independent claims 1 or 24.

Claim 11 depends directly from claim 1, and claim 27 depends directly from claim 24. As such, Applicants respectfully submit that these claims are not anticipated by the Fine reference for at least the above-cited reasons. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejection of claims 1, 11, 24 and 27 based upon the Fine reference. Claim 3 has been cancelled by way of the present communication and, accordingly, the rejection of this claim has been rendered moot.

D. Anticipation Rejections based on the Moore Reference (U.S. Patent 6,727,073).

Claims 1 and 3 have been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,727,073 to Moore et al. (hereinafter the "Moore reference"). *See*, Office Action at page 16, ¶ 29. As the Moore reference fails to describe, either expressly or inherently, each and every element as set forth in the rejected claims, Applicants respectfully traverse this rejection.

The Office Action rejected claims 1 and 3 on the grounds that the Moore reference disclosed a method comprising "obtaining a fecal sample . . . measuring the sample to see if it contains an elevated level of lactoferrin . . . and [diagnosing irritable bowel syndrome for] a sample that is negative [for an elevated level of lactoferrin]." *See Office Action dated 7/15/2008*, page 16. In addition to the fact that each claim element was not rejected in the Office Action, the Moore reference does not describe each claim element.

As previously discussed, amended claim 1 requires determining that a sample contains an elevated level of ASCA or ANCA and diagnosing the person from whom the sample was obtained based upon such determination. The Moore reference, on the other hand, is directed to a method for determining and diagnosing inflammatory enteric disease using an immunochromatographic test device having a multiplicity of test zones. *See* Moore reference at Abstract. The inflammatory enteric disease markers tested for are fecal lactoferrin, a bacteria marker, a virus marker, and a protozoa marker. *See id.* The Moore reference does not describe, either expressly or inherently determining whether the obtained fecal sample contains an elevated level of either ASCA and ANCA, nor does it disclose diagnosing a patient based upon elevated levels of either ASCA or ANCA. As such, it is respectfully submitted that the More reference fails to anticipate independent claim 1. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejection of claim 1 based upon the Moore reference. Claim 3 has been cancelled by way of the present communication and, accordingly, the rejection of this claim has been rendered moot.

Rejections based on 35 U.S.C. § 103(a)

A. Applicable Authority.

Title 35 U.S.C. § 103(a) declares, a patent shall not issue when "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." The Supreme Court in *Graham v. John Deere* counseled that an obviousness determination is made by identifying: the scope and content of the prior art; the level of ordinary skill in the prior art; the differences between the

claimed invention and prior art references; and secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1 (1966).

To support a finding of obviousness, the initial burden is on the Office to apply the framework outlined in *Graham* and to provide some reason, or suggestion or motivation found either in the prior art references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the prior art reference or to combine prior art reference teachings to produce the claimed invention. See, *Application of Bergel*, 292 F. 2d 955, 956-957 (1961). Thus, in order "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success [in combining the references]. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." *See* MPEP § 2143. Recently, the Supreme Court elaborated, at pages 13-14 of *KSR*, it will be necessary for [the Office] to look at interrelated teachings of multiple [prior art references]; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by [one of] ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the [patent application]." *KSR v. Teleflex*, 127 S. Ct. 1727 (2007).

B. Rejections Based on the Nielsen Reference in view of the Targan Reference and the Fine (2) Reference.

Claims 1-3, 6-10, 24 and 27 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Nielsen et al., *The American Journal of Gastroenterology*, Vol. 95, No. 2,

359-367, 2000 (hereinafter the "Nielsen reference"), in view of Targan et al., *Journal of Immunology*, 1995, Vol. 155, Issue 6, 3262-3267, 1995 (hereinafter the "Targan reference") and Fine, PG – Pub 2001/0036639A1, filing date March 2, 2001 (hereinafter the "Fine (2) reference"). Applicants submit the a prima facie case of obviousness of the rejected claims cannot be established based upon the asserted combination of references due to significant differences between the cited references and the claimed invention, as more fully described below.

Independent claim 1, as amended herein, is directed to a method for testing fecal samples from persons for diagnosis. The method comprises obtaining a fecal sample from a person presenting with symptoms common to inflammatory bowel disease and irritable bowel syndrome, determining that the sample contains an elevated level of lactoferrin, and measuring the sample for an elevated level of anti-*Saccharomyces cerevisiae* antibodies (ASCA) and an elevated level of anti-neutrophil cytoplasmic antibodies (ANCA). Upon determining that the sample has an elevated level of anti-*Saccharomyces cerevisiae* antibodies and not an elevated level of anti-neutrophil cytoplasmic antibodies, the patient is diagnosed with Crohn's disease. In contrast, upon determining that the sample has an elevated level of anti-neutrophil cytoplasmic antibodies and not an elevated level of anti-*Saccharomyces cerevisiae* antibodies, the patient is diagnosed with ulcerative colitis.

Independent claim 24, as amended herein, is directed to a method for distinguishing inflammatory bowel disease from irritable bowel syndrome and for differentiating ulcerative colitis from Crohn's disease. The method comprises obtaining a fecal sample from a person presenting with symptoms common to inflammatory bowel disease and irritable bowel syndrome and measuring the sample for an elevated or non-elevated level of lactoferrin. Upon

determining that the sample has a non-elevated level of lactoferrin, the person is diagnosed with irritable bowel syndrome. Conversely, upon determining that the sample has an elevated level of lactoferrin, the sample is selected for further measurements. The selected sample is measured for an elevated level of anti-*Saccharomyces cerevisiae* antibodies (ASCA) and an elevated level of anti-neutrophil cytoplasmic antibodies (ANCA). Upon determining that the selected sample has an elevated level of anti-*Saccharomyces cerevisiae* antibodies and not an elevated level of anti-neutrophil cytoplasmic antibodies, the patient is diagnosed with Crohn's disease. In contrast, upon determining that the selected sample has an elevated level of anti-neutrophil cytoplasmic antibodies and not an elevated level of anti-*Saccharomyces cerevisiae* antibodies, the patient is diagnosed with ulcerative colitis.

Applicants submit that none of the cited references, whether taken alone or in combination, teaches or suggests diagnosing Crohn's disease for the person having a sample with an elevated level of anti-*Saccharomyces cerevisiae* antibodies (ASCA) and diagnosing ulcerative colitis for the person having a sample with an elevated level of anti-neutrophil cytoplasmic antibodies (ANCA).

Rather, the Nielsen reference discloses testing for ASCA and ANCA in serum. *See,* Nielsen reference at page 361. The Nielsen reference does not teach or suggest testing a fecal sample for an elevated level of ANCA or ASCA. Furthermore, the Nielsen reference does not teach diagnosing Crohn's disease for a person that has an elevated level of ASCA in a fecal sample or diagnosing ulcerative colitis for a person that has an elevated level of ANCA in a fecal sample.

Further, the Targan reference does not cure these noted deficiencies of the Nielsen reference. Like the Nielsen reference, the Targan reference discloses determining the presence

of ANCA or ASCA in a serum sample. *See* Targan reference at page 3262. The Targan reference does not teach diagnosing a person with an elevated level of ASCA with Crohn's Disease. Furthermore, there is no teaching or suggestion in the Targan reference of what an elevated level of ANCA in a fecal sample is. The Targan reference does not teach that ANCA crosses through the intestinal wall from the serum in such an amount to diagnosis ulcerative colitis for a person having an elevated level of ANCA in a fecal sample.

Likewise, the Fine (2) reference does not teach or suggest diagnosing ulcerative colitis for a person having a sample with an elevated level of ANCA. Rather, the Fine (2) reference teaches a method for diagnosing food sensitivities. The Fine (2) reference does not teach or suggest diagnosing Crohn's disease if a fecal sample contains an elevated level of anti-*saccharomyces cerevisiae* antibodies. Rather, the Fine (2) reference teaches a method for diagnosing food sensitivities. Crohn's disease is not a food sensitivity to anti-*Saccharomyces cerevesiae*. The Fine (2) reference does not teach or suggest that an elevated level ASCA in fecal sample can be used to diagnose Crohn's disease or that an elevated level of ANCA can be used to diagnose ulcerative colitis.

Additionally, it would not be obvious to one of skill in the art to combine the cited references to make the claimed invention. Just because a marker may be contained in some level in a fecal sample, does not make it obvious that it would occur in an amount that is measurable in order to diagnose a particular disease state, *e.g.*, diagnosing Crohn's disease for a person having a fecal sample with elevated ASCA. Furthermore, just because a cut-off level can be determined in serum to diagnose a disease does not make it applicable to a fecal sample. Human serum varies greatly from human feces. One of skill in the art can appreciate that human feces varies greatly in consistency and make-up based upon the human diet, health and lifestyle much more

so than human serum varies based on these factors. As such, it would not have been obvious to one of skill in the art that a cut-off level to define an elevated level of a marker, such as ASCA, actually could be determined in feces based on results of testing done for serological markers.

With further respect to claim 24, distinguishing between IBD and IBS is recited. When a patient presents with symptoms common to IBD and IBS, it is difficult to distinguish between the two conditions. Claim 24 relates to diagnosing IBS when a patient presents with symptoms common to IBD and IBS if the level of fecal lactoferrin is not elevated for the patient. The cited references, alone or in combination, do not teach this. Specifically, the Nielsen, Targan and Fine (2) references do not teach measuring the level of lactoferrin in patients with IBS. It was unknown whether patients with IBS had elevated levels of lactoferrin. More specifically, while the Nielsen reference teaches that fecal lactoferrin may be utilized as a marker for disease activity in IBD, it is silent as to whether patients with IBS have elevated levels of lactoferrin.

The Targan and Fine (2) references do not cure this deficiency as they also fail to teach or suggest diagnosing IBS when a person presents with symptoms common to IBD and IBS if the level of fecal lactoferrin is not elevated for the patient. The Targan reference determines the presence of ANCA in a serum sample and does not discuss determining the level of lactoferrin in a fecal sample. *See*, Targan reference at Page 3262. The Fine (2) reference teaches a method for diagnosing food sensitivities and does not discuss determining the level of lactoferrin in a fecal sample.

Applicants submit that the Nielsen reference in view of the Targan reference in view of the Fine (2) reference neither teaches nor suggests all the claim limitations of independent claims 1 and 24. As such, it is respectfully submitted that a prima facie case of

obviousness under 35 U.S.C. § 103(a) cannot be established based upon the asserted combination of references. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection of these claims. As each of claims 2, 6-10 and 27 depends from one of independent claims 1 and 24, Applicants request withdrawal of the 35 U.S.C. §103(a) rejection of these claims as well for at least the above-cited reasons. *See, In re Fine*, 5 USPQ 2d 1596, 1600 (Fed. Cir. 1988) (a dependent claim is obvious only if the independent claim from which it dependents is obvious); *see also*, MPEP § 2143.03. Claim 3 has been cancelled by way of the present communication and, accordingly, the rejection of this claim has been rendered moot.

CONCLUSION

For at least the reasons stated above, claims 1, 2, 6-12, 15-17, 20, 24, and 27 are believed to be in condition for allowance. Applicants respectfully request withdrawal of the pending rejections and allowance of the claims. If any issues remain that would prevent issuance of this application, the Examiner is urged to contact the undersigned – 816-474-6550 or twilhelm@shb.com (such communication via email is herein expressly granted) – to resolve the same.

The fee for three-month extension of time is submitted herewith. It is believed that no additional fee is due. However, if this belief is in error, the Commissioner is hereby authorized to charge any amount required, or credit any overpayment, to Deposit Account No. 19-2112, referencing attorney docket number TLAB.100292.

Respectfully submitted,

/Tawni L. Wilhelm/

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